

Application No. 10/516,419
Reply to Office Action of November 3, 2009

Docket No.: 60008(49991)

and wherein the non-proteinaceous small molecule is not a peptide.

REMARKS

Claims 1-16 and 52 are pending in this application. Claims 1 and 52 have been amended. Accordingly, Claims 1, 3-16 and 52 will be pending in the Application upon entry of the Claim Amendments presented herein.

Claims 1 and 52 have been amended to recite that the non-proteinaceous small molecule is not a peptide. Support for this amendment can be found throughout the Specification as originally filed; in particular, at least, for example, at Page 6, line3. No new matter has been added.

Amendment of the Claims is not to be construed as acquiescence to any objections/rejections set forth in the pending Office Action, or any previous Office Action, and was done solely to expedite prosecution of the Application. Applicants respectfully reserve the right to pursue any non-elected, canceled, or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

References listed on SB-08

The Examiner has requested the publication date and relevance of Reference CA listed on the SB-08. Applicants note that the document was published in 2007.

The Examiner has also requested a statement of relevance with regard to Polish Patent No. PL-175563. Applicants note that this document was originally cited, without comment, by Examiner Alex Noguerola in application No. 10/169,002 now U.S. Patent No. 7,229,539, in connection with a Non-Final Office Action. The CA PLUS Abstract which Examiner Noguerola is attached hereto to supplement the Patent Document submitted. The Examiner contended that the reference was relevant based on the surfactant of formulas I and II as described in the CA PLUS Abstract.

Rejections under 35 U.S.C. § 103(a)

Claims 1-16, and 52 are rejected under 35 U.S.C. 103 (a), as unpatentable over the combination of PCT International Patent Publication No. WO 00/70334A1 to Lee (“Lee”) in view of United States Published Patent Application No. US 2005/0153346 to Schneider (“Schneider”). Applicants respectfully disagree and traverse the rejection.

Claim 1 recites a method for analysis of a non-proteinaceous small molecules comprising contacting a biological sample; said sample containing at least one non-proteinaceous small molecule with a surfactant wherein the analysis comprises dissociation of a non-proteinaceous small molecule from a biological sample and wherein the non-proteinaceous small molecule is not a peptide. As discussed in prior responses, Lee describes the analysis of large molecules, *specifically proteins or peptides*. The Examiner alleges that Lee, in teaching the potential use of MALDI, shows that is desirable to use the elected surfactant to improve the analysis of “digests” and equates the presumed “digests” of Lee with non-proteinaceous small molecules.

Indeed, as discussed in the interview, Lee is focused primarily on the analysis of entire proteins. As all of the large molecules of Lee are *proteinaceous, i.e. proteins or peptides*, any MALDI digests of Lee would also be *proteinaceous*.

As such, Applicants contend nothing in Lee teaches or suggests the analysis of non-proteinaceous small molecules. Even if one were to read the digests of Lee as to teach non-proteinaceous small molecules, at best Lee would only teach the analysis of peptides. Moreover, there is no teaching or suggestion in Lee of the dissociation of a non-proteinaceous small molecule from the protein binding effect of a biological sample.

Schneider does nothing to rectify the deficiencies of Lee. Schneider merely describes the use of MALDI for the analysis of different sized molecules. Indeed, a careful reading of Schneider would lead one of ordinary skill in the art away from the Examiner’s assertion that MALDI analysis would digest large molecules into small molecules as Schneider states that MALDI is one of “the best able to *ionize large, low volatility molecular species*.” (See, Paragraph 125, emphasis added). As such, even if one of ordinary skill were to look to Schneider for the teaching that MALDI can be used for non-proteinaceous small molecular species, the same artisan would have been taught that *proteinaceous large molecules are ionized* by MALDI and not digested into non-proteinaceous small molecular species. Again, even if one were to read Schneider to include the digestion of proteinaceous large molecules, at best, Schneider would only teach the analysis of peptides. There is no teaching or suggestion in Schneider of the dissociation of a non-proteinaceous small molecule from the protein binding effect of a biological sample.

Thus, one of ordinary skill would have had no motivation to combine the MALDI teachings of Schneider with large proteinaceous molecular analysis of Lee, let alone modify those teachings to arrive at the small molecule analysis method of the claimed invention.

Even if one of ordinary skill in the art were motivated to combine the references, Applicants respectfully submit that he would have lacked the necessary expectation of success in utilizing a surfactant as described by Lee for the analysis of one or more non-proteinaceous small molecules contained within a sample such that the small molecule is dissociated from the biological sample. At best, one of ordinary skill in the art may have expected the surfactant to assist in the analysis of proteins or peptides found in the sample, as surfactants have historically been used only for the analysis of similar large molecules due to their binding characteristics. (See background section of Application.)

Finally, as previously argued and discussed above, the effect of the use of the surfactant disclosed in the present invention has a surprising and unexpected result of releasing a small molecule from a biological sample for analysis. In particular, the surfactants provided by the present invention surprisingly and unexpectedly avoid the protein binding of small molecules in a biological sample associated with other surfactants such as SDS. As a result of this invention, near complete recovery of a small molecule in a biological sample can be obtained without further ion suppression upon analysis thereby allowing for determination of small molecule in a sample in total, free form and bound form. See, for example, Comparative Example 2 and the data presented in Figure 1.

Assuming for the sake of argument that the Office Action has made out a *prima facie* showing of obviousness based on the cited combination of records, M.P.E.P. §2144.05 indicates that “[a] *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997)”. In view of the unexpected and surprising result afforded by the claimed invention and the teaching away in Schneider, Applicants have rebutted any *prima facie* showing of obviousness if such a showing had been made.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103 of Claims 1-16 and 52.

Double Patenting rejections

Claims 1-16 and 52 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over Claims 1, 3-5, 7-9, 11, 13-18, 20-30, 33, and 123 of U.S. Patent Application Serial No. 10/516,418. Similarly, Claims 1-16 and 52 are rejected on

the grounds of nonstatutory obviousness-type double patenting over claims 1-7 and 13-20 of U.S. Patent No. 7,229,539.

As it remains unknown what subject matter claimed and disclosed in the present application will be deemed allowable any statement regarding these rejections made on Applicants' part is premature. Therefore, Applicants respectfully request that these rejections be held in abeyance until subject matter is deemed allowable in this application.

CONCLUSION

In view of the remarks made herein, Applicants submit that the application is in condition for allowance, and respectfully request favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicant's representative would be helpful in resolving any remaining issues and/or expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number indicated below before issuance of the next office action. Applicants thank the Examiner in advance for this courtesy.

Applicants believe that no additional fees, other than the fee for the two-month extension of time, are required in connection with this paper. Nevertheless, Applicants authorize the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 60008US(49991).

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Respectfully submitted,

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